specification was considered informal in the arrangement of subheadings. Claims 1-29, 36, and 40-42 stand rejected under 35 U.S.C. § 112, first paragraph. Claims 1-29, 36, and 40-42 stand rejected under 35 U.S.C. § 112, second paragraph. Claims 17-21 stand rejected under 35 U.S.C. § 101. Claims 1, 2, 4-13, 15-29, 36, and 40-42 stand rejected under 35 U.S.C. § 102(b). Claims 1-4, 6-24, 26, 28-29, 36, and 40-42 stand rejected under 35 U.S.C. § 102(e). Claims 1-4, 6-29, 36, and 40-42 stand rejected under 35 U.S.C. § 103(a). Each of these objections and rejections is addressed as follows.

Objections under 37 C.F.R. § 1.75(c)

Claims 13-29, 36, and 40-42 were objected to under 37 C.F.R. § 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative. This rejection has been met by the present amendment to each of these claims, which incorporates the language "any one of claims." Claims 17-29 were further rejected on the basis of minor informalities, all of which have been corrected by the present claim amendments.

Specification

The Examiner has indicated that the application is informal in the arrangement of the specification and has therefore requested that the specification be amended to include the section subheadings: "Brief Description of the Drawings" and "Detailed Description

of the Invention." By the present amendment to the specification, applicants have complied with this request.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 1-29, 36, and 40-42 stand rejected, under 35 U.S.C. § 112, first paragraph, on the basis that the disclosure in applicants' specification (1) fails to provide a written description of the claimed invention and (2) is not commensurate in scope with the claimed invention. For the following reasons, each of these rejections is respectfully traversed.

Written Description

Claims 1-29, 36, and 40-42 stand rejected, under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to convey to one skilled in the relevant art that the inventors had possession of the claimed invention. More specifically, the Office Action asserts that, because applicants have described only a single genomic clone (and its respective cDNA clone) from *Arabidopsis* which encodes an acquired resistance polypeptide, it is not clear that applicants were in possession of the invention as broadly claimed. To support this assertion, the Office relies on the Federal Circuit's opinion in *Univ. of California. v. Eli Lilly and Co.,* 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997) for the proposition that :

> [T]he disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite disclosure of a cDNA encoding that protein from another organism.

This ground for the rejection is respectfully traversed.

To provide an adequate "written description," applicants need only communicate to those skilled in the art that the claimed subject matter is intended to be part of their invention. As stated by the Federal Circuit in *Martin v. Mayer*, 823 F.2d 500, 3 U.S.P.Q.2d 1333 (Fed. Cir. 1987):

> [T]he specification must 'convey clearly to those skilled in the art to whom it is addressed...the information that [the inventor] has invented the specific subject matter later claimed.'

Moreover, the MPEP § 2163.02 (Rev. 3, July 1997) states:

> [A]n objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed (emphasis added)."

Applicants have met these standards since the present specification would certainly indicate to one of ordinary skill in the art that applicants discovered a family of related nucleic acid molecules encoding ankyrin repeat-containing disease resistance polypeptides, as currently claimed.

On this point, the Examiner's attention is directed to applicants' specification, for example, at page 6 (lines 11-12) and page 43 (line 28) - page 44 (line 9), where applicants

describe the claimed class of acquired resistance genes and their shared, characteristic ankyrin repeats. Based on this description and other statements contained within the specification, one skilled in the art would recognize and appreciate that applicants had indeed invented the scope and content of the presently claimed invention. In particular, applicants submit that, even though the claimed invention is exemplified by the *Arabidopsis* NPR1 and *Nicotiana glutinosa* NPR1 homolog described in the present specification, one of skill in the art reading this specification would have readily recognized that these genes were merely provided for the purpose of illustrating the invention and that applicants' invention included any acquired resistance gene encoding a disease resistance polypeptide having an ankyrin repeat. It is this description that also allows the skilled worker to identify and recognize other species falling within the present claims.

Moreover, applicants submit that their specification provides a written description of the presently claimed invention in sufficient detail to satisfy the standard set by the Federal Circuit in *Lilly,* 43 USPQ2d 1398. In particular, this case specifically states that the written description of a genus of DNA may be achieved by a "recitation of structural features common to members of the genus." *Lilly,* 43 USPQ2d 1398, 1406.

Applicants point out that, contrary to the assertion in the present Office Action, the description of the claimed invention in applicants' specification does not rely simply on the disclosed sequence of the *Arabidopsis* NPR1 gene. Rather, the present specification

describes a novel class of plant disease resistance genes on the basis of a specific structural feature—an ankyrin repeat motif—common to the members of this family. Applicants' specification therefore provides a description of the class of DNA molecules encompassed by the present claims in a form entirely consistent with the standard set out in *Lilly*, and, on this basis, the § 112 rejection should therefore be withdrawn.

Scope of Enablement

Claims 1-29, 36, and 40-42 also stand rejected under § 112, first paragraph based on the assertion that the teachings of applicants' specification is not commensurate in scope with the present claims. More specifically, the Office Action states:

> [T]he state of the art for isolation of cDNA or genomic clones with a defined functionality is highly unpredictable. Significant guidance is required with regard to hybridization/wash conditions or PCR reaction conditions that will allow specific isolation of the target genes. Applicant has characterized and isolated a single acquired resistance gene from *Arabidopsis*, and provided general guidance for hybridization and PCR techniques. Although Applicant describes isolation of a structurally related gene from *Nicotiana glutinosa* by hybridization with the *NPR1* cDNA, the hybridization conditions are not high stringency (see Specification, p. 49, lines 18-20 as compared to the definition of high stringency at p. 51, lines 13-21), and Applicant does not provide any evidence to support the functional relatednesss of the *Nicotiana* cDNA to the *NPR1* gene. The novelty of the instant invention is the isolation of a gene which plays a functional role in the acquired resistance response in plants. Applicant has not precisely defined the function of the *NPR1* gene, nor has Applicant provided any guidance with respect to the structural and functional similarity of related genes among different plant species. In the absence of such guidance, and in the absence of specific evidence regarding the functional role of the isolated *Nicotiana* cDNA or guidance with respect to

> hybridization/wash conditions which would allow specific isolation of nucleic acid molecules from other plant species which are functionally related to *NPR1*, undue trial and error experimentation would be required to screen through the vast number of cDNA and genomic clones from *Arabidopsis* or another plant species, to identify those that are functionally related to *NPR1* and also play a role in acquired resistance in plants.

For the following reasons, applicants respectfully traverse this ground for the rejection.

Applicants first point out that the Federal Circuit has made clear the level of teaching needed to enable a claim with respect to the prior art, and has stated that a patent need not reiterate techniques known to skilled workers in a particular area of technology. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 231 USPQ 81 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed Cir. 1988); *Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 3 USPQ2d 1737 (Fed. Cir. 1987), *cert. denied*, 484 U.S. 954 (1987) ("A patent need not teach, and preferably omits, what is well known in the art."); *see also Paperless Accounting, Inc. v. Bay Area Rapid Transit Sys.*, 804 F.2d 659, 231 USPQ 649 (Fed. Cir. 1986) ("A patent applicant need not include in the specification that which is already known to and available to the public.").

In view of this standard, applicants submit that, given the teaching of the specification and the level of skill in the art at the time the present application was filed, (1) one skilled in the art would have reasonably understood how to isolate additional genes falling within the scope of the present claims using standard gene cloning methods

and (2) the determination of whether such genes conferred disease resistance on a transgenic plant would not constitute undue experimentation.

First, applicants point out that, having access to applicants' newly disclosed ankyrin repeat-containing acquired resistance gene sequence, one skilled in the art could find additional nucleic acid molecules encoding such disease resistant polypeptides from virtually any plant absent "undue experimentation," simply by following the teachings found in applicants' specification in combination with standard methods known in the art at the time of applicants' invention. On this point, the Examiner is referred to the case of *In re Wands* (858 F.2d 731, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988)), which sets forth the CAFC standard for enablement in the biotechnology arts. *Wands* holds that an invention is enabled so long as the teaching of the specification provides the invention without undue experimentation. *Wands* states that:

> the test [for determining whether experimentation is undue] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed (emphasis added).

Applying this standard to the present case, it is clear that applicants' specification satisfies this first test outlined by the CAFC in *Wands*. According to *Wands*, a considerable amount of experimentation is permissible, if it is merely routine. Looking to applicants' situation, any "experimentation" involved in isolating and characterizing additional nucleic acid molecules falling within the present claims is straightforward, and

is rendered so by applicants' discovery of the sequence encoding the *NPR1* gene. Specifically, if one skilled in the art wished to isolate homologous disease resistance sequences from other plant species, they would simply use applicants' disclosed nucleotide sequences (for example, the *NPR1* sequence) as a probe in combination with conventional methods, such as hybridization or PCR amplification. Contrary to the Examiner's assertion, these approaches would require only standard applications of hybridation wash conditions or PCR amplification techniques, and possibly the type of empirical condition adjustments carried out routinely, and successfully, by molecular biologists in isolating gene families. Accordingly, there is no basis for concluding that one skilled in the art, equipped with applicants' sequences and standard methods known in the art, would not be able to isolate a reasonable number of related resistance genes falling within the scope of the present claims.

Alternatively, applying the second test of *Wands*, a "reasonable amount of guidance" is also provided by applicants' specification. For example, applicants outline general methods useful for identifying and characterizing DNAs encoding additional resistance gene sequences, for example, at pages 50-53, and also provide exemplary oligonucleotide primers for use in connection with these methods. Furthermore, as described on pages 49-50, applicants teach the sequence of an *NPR1* homolog isolated from tobacco. As is noted in the specification at page 49 (lines 6-9), this homolog was isolated using standard hybridization techniques. Moreover, like the *Arabidopsis NPR1*

gene, the *Nicotiana glutinosa NPR1* homolog encodes a gene product possessing an ankyrin repeat motif (see, e.g., amino acids 264-392 of the deduced amino acid sequence of the tobacco polypeptide shown in Fig. 7B). In view of this evidence, applicants submit that the present specification certainly provides guidance for the screening of recombinant libraries to identify other DNAs encoding disease resistance polypeptides having ankyrin repeats and that this teaching, in and of itself, is more than adequate to satisfy the requisite "reasonable amount of guidance." Accordingly, based on this second test as well, applicants submit that the present specification is within the bounds set out by *Wands* for an enabling disclosure.

In sum, armed with applicants' teachings and the disclosed *NPR1* genes, it would be a trivial matter to isolate additional genes from other plants using the methods outlined in the specification. Any "experimentation" involved would be entirely straightforward and routine. Applicants therefore maintain that their specification satisfies the enablement standard under, not one, but both of the alternative tests set forth by *Wands*.

Turning to the assertion that screening of genomic or cDNA libraries constitutes undue trial and error experimentation, applicants point out that those of skill in the art of molecular biology have long been aware that the isolation and sequence determination of a particular gene necessitates the screening of a recombinant cDNA or genomic library in order to obtain a clone having the specific desired characteristics (e.g., a plant resistance gene sequence expressing a polypeptide including an ankyrin repeat). Such screening,

despite its time-consuming nature, does not constitute undue experimentation under the law. Methods for screening recombinant libraries, as well as methods for determining the sequence of an isolated clone, had been routinely used in the art for over 15 years prior to applicants' filing date. For example, in 1975 and 1977, Grunstein and Hogness[1] and Benton and Davis,[2] respectively, provided methods for isolating specific genes from recombinant libraries, and, by at least 1977, Sanger, Nicklen, and Coulson[3] enabled methods for determining the DNA sequences of such isolated genes.

As the case of *In re Wands* (858 F.2d 731, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988)) makes clear, enablement is not negated by the necessity for some experimentation such as routine screening. The nature of molecular biology is that it involves screening recombinant libraries to determine which clone within a library contains the gene with the desired characteristics. Like the practitioners of the monoclonal antibody art described in *Wands*, who screened many hybridomas to isolate the one having the desired characteristics, practitioners in the art of molecular biology are prepared to screen many clones to find one that contains a desired gene. Screening of a recombinant library to

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[1] Grunstein and Hogness, Colony hybridization: A method for isolating of cloned DNAs that contain a specific gene. *Proc. Natl. Acad. Sci. U.S.A.* 72: 3961, 1975.

[2] Benton and Davis, Screening λgt recombinant clones by hybridization to single plaques *in situ*. *Science* 196: 180, 1977.

[3] Sanger, Nicklen, and Coulsen, DNA sequencing with chain-terminating inhibitor. *Proc. Natl. Acad. Sci. U.S.A.* 74: 5464, 1977.

isolate a plant disease resistance gene sequence falling within applicants' claims is considered to be a routine step in the process of isolating a gene having desired characteristics; it cannot constitute undue experimentation.

Finally, with respect to determining the function of a candidate disease resistance gene, applicants point out that one skilled in the art could easily test whether such a gene that was isolated from standard screens (as discussed above) conferred disease resistance. For example, at pages 44-47 and 65-67 of the specification, applicants disclose exemplary assays useful for determining whether a candidate nucleic acid molecule confers a disease resistance phenotype. Applicants' specification provides clear scientific evidence, for example, that the *NPR1* gene confers resistance against both bacterial and fungal pathogens (see, e.g., pages 44-45). Moreover, applicants demonstrated that *NPR1* mutations in an ankyrin repeat resulted in plants having enhanced susceptibility to pathogen infection. In view of these experiments, it is clear that, to test a candidate gene for disease resistance capabilities, one need only prepare a transgenic plant expressing the candidate DNA sequence and then determine whether its expression results in disease resistance, for example, by determining the response of the transgenic plant to one or more pathogens, exactly as described by applicants in their specification.

Applicants also point out that, to sustain an enablement rejection, the Office has the initial burden to establish a reasonable basis to question the enabling nature of an applicant's specification. Thus, in a case in which the PTO questions the enablement of a

claim, the CCPA, in *In re Marzocchi*, 439 F.2d 220, 169 USPQ 367, 369 (CCPA 1971) has stated that:

> a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support (emphasis added).

The MPEP (§ 2164.04, Rev. 3, July 1997) further emphasizes the *Marzocchi* standard in stating that:

> it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure (emphasis added).

Here, applicants note that no scientific evidence currently made of record in this case establishes a basis for doubting the objective truth of the statements found in applicants' specification regarding enablement with respect to isolating genes falling within applicants' claims and determining whether such genes possess disease resistance properties. As is discussed above, applicants' statement that expression of an acquired resistance gene encoding a polypeptide possessing an ankyrin repeat confers pathogen resistance on host plants is in accordance with the evidence described in the present specification for the *NPR1* gene. Moreover, the Examiner has provided no evidence or

reason for doubting applicants' statement that other genes having the structural features described by applicants would function similarly as disease resistance genes. On this basis, as well, the facts in the present case compel withdrawal of the § 112, first paragraph enablement rejection, and applicants request reconsideration on this issue.

Claim 36 also stands rejected under § 112, first paragraph. In particular, the Office Action states:

> Claim 36 reads on a method of producing an acquired resistance polypeptide in a cell *in vivo*, which in turn reads on gene therapy. Applicant has clearly not provided guidance for expression of an acquired resistance gene in a mammal, for example. The scope of the claims should be limited to the teachings of the specification, and hence should be limited to a host cell in culture.

This rejection is respectfully traversed.

Applicants point out that claim 36, in fact, requires the culturing of a transformed cell expressing the nucleic acid molecule of the invention, as well as the recovery of the expressed acquired resistance polypeptide. Accordingly, claim 36 does not read on gene therapy. Reconsideration on this issue is requested.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 1-29, 36, and 40-42 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention, which are addressed as follows.

Claim 1 was deemed indefinite in reciting the term "including." This rejection has been met by the present amendment to claim 1 in which this term has been deleted.

Claim 1, as well as claims 10-12 and claim 36, have been rejected as indefinite in reciting the phrase "acquired resistance polypeptide." More specifically, the Office Action states:

> [T]he phrase is not defined in the Specification, however, Applicant defines "acquired resistance gene" to mean "a gene encoding a polypeptide capable of triggering a plant acquired resistance response (for example, a systemic acquired resistance (SAR) or local acquired resistance response (LAR) in a plant cell or plant tissue" (Specification, p. 9, lines 22-25). However, it is not clear what is encompassed by a "plant acquired resistance response," whether it means increased pathogen resistance, increased PR gene expression, increased response to SA or INA, or some other response. SAR and LAR are complex phenomena in plants and involve a host of different signal transduction pathways, transcriptional regulatory mechanisms, and phenotypic effects. Many of the molecules and pathways involved in SAR and LAR also play roles in other plant developmental or biochemical pathways. Hence, it is not known what responses, and hence what isolated nucleic acid molecules, are encompassed by the claims.

Applicants' specification makes clear the meaning of a "plant acquired resistance response" by clear reference to the SAR (systemic acquired resistance) and LAR (local acquired resistance) responses — two disease resistance responses that are extraordinarily well known in the art. Given the context of "plant acquired resistance response," applicants submit that this phrase is, in fact, definite and is entirely consistent with usage in this area of technology. In view of this guidance and the understood meanings of both SAR and LAR and usage by those skilled in the art, applicants request reconsideration

and withdrawal of this basis for the indefiniteness rejection as applied to claims 1, 10-12, and 36.

Claim 1 was also deemed indefinite in reciting the phrase "being capable of conferring." This rejection has been met by the present amendment to claim 1 in which this phrase has been replaced with the term "confers."

Claim 2 was deemed indefinite in reciting the phrase "is capable of meditating" because it is unclear whether or not the polypeptide mediates expression. This rejection has been met by the present amendment to claim 2 in which this phrase has been replaced with the term "activates."

Claim 4 was deemed indefinite in the recitation of the phrase "polypeptide obtained from." This rejection has been met by the present amendment to claim 4 in which this phrase has been replaced with the phrase "isolated nucleic acid molecule is derived from."

Claims 10-12 were deemed indefinite in reciting the term "that" because it is not clear whether the term refers to the nucleic acid molecule or the polypeptide. This rejection has been met by the present amendment to these claims suggested by the Examiner, which replace the term with the phrase "and that."

Claims 10-12 were also deemed indefinite in reciting the phrase "specifically hybridizes to." In particular, the Office Action contends that the phrase is indefinite because "it is not clear what is encompassed by the claim, *i.e.* those nucleic acid

molecules which hybridize under low stringency conditions, or those which hybridize under high stringency conditions." This rejection is respectfully traversed.

As an initial matter, applicants point out that the phrase "specifically hybridizes" is perfectly clear and unambiguous in view of the specification and what was known in the art. According to § 2173.05(a) of the MPEP (Rev. 3, July 1997), "[T]he meaning of every term used in a claim should be apparent from the prior art or from the specification and drawings at the time the application is filed." Low and high stringency hybridization conditions are terms of art plainly recognized when it comes to understanding whether one nucleic acid molecule specifically hybridizes to another. Furthermore, a skilled worker would have no trouble understanding such terms in the context of the present invention.

In addition, applicants point out that, according to MPEP § 2173.04 (Rev. 3, July),

> [B]readth of a claim is not to be equated with indefiniteness. *In re Miller*, 441 F.2d 689, 169 USPQ 597 (CCPA 1971). If the scope of the subject matter embraced by the claims is clear...then the claims comply with 35 U.S.C. 112, second paragraph.

The scope of the claimed subject matter embraced by claims 10-12 is clear and definite: the claim reads on any nucleic acid encoding an acquired resistance polypeptide including an ankyrin repeat which specifically hybridizes under low stringency or high stringency conditions, to the nucleic acid molecules isolated by applicants. Indeed, one skilled in the art having knowledge of the principles of hybridization between complementary

polynucleotides would readily understand that specific hybridization can occur under either low and high stringency conditions, as described in applicants' specification. Accordingly, applicants' description of different low and high stringency hybridization conditions is entirely consistent with art recognized procedures involving hybridization analyses. Given this description, one of ordinary skill in the art would clearly understand the scope and content of claims 10-12.

Furthermore, the patent law does not require that all possible permutations of hybridization conditions be listed in the patent, let alone be listed in the claims, as seemingly required in this instance. *See Orthokinetics, Inc. v. Safety Travel Chairs, Inc.* 806 F.2d 1565, 1 USPQ2D 1081 (Fed. Cir. 1986) ("As long as those of ordinary skill in the art realized that the dimensions could be easily obtained, § 112, second paragraph requires nothing more.")

For all of the above reasons, the § 112, second paragraph rejection of claims 10-12 may be withdrawn.

Claim 13 was deemed indefinite in reciting the term "mediates," with the Office Action stating that there are many different ways that expression may be mediated. This rejection has been met by the present amendment to claim 2 in which this phrase has been replaced with the term "activates."

Claim 16 was deemed indefinite in reciting the phrase "being capable of directing expression." This rejection has been met by the present amendment to claim 16 in which

this phrase has been replaced with the phrase "directing expression."

Claims 17, 22, 36, and 40 were deemed indefinite as lacking proper antecedent basis because claim 16 is drawn to a vector, and not to a nucleic acid molecule. This rejection has been met by the present amendment to these claims in which the phrase "a vector of claim 16" has been included to provide antecedent basis regarding reference to claim 16.

Claims 24 and 27 were deemed indefinite because the phrase "said transgenic angiosperm" lacks proper antecedent basis. These rejections have been met by the present amendment to claim 23, which refers to a transgenic angiosperm, and to claim 24, in which the dependency of this claim has been corrected to provide proper antecedent basis.

Claim 36 was deemed indefinite in reciting the phrase "providing a cell transformed," with the Office Action asserting that this phrase fails to connote an active method step. Applicants contend that this phrase does in fact constitute an active method step since an individual practicing the invention might have obtained a cell that was previously transformed with a DNA of the invention, requiring simply the step of expressing the DNA and isolating the expressed polypeptide. This rejection should therefore be withdrawn.

Claim 36 was also deemed indefinite in reciting the phrase "positioned for expression in the cell." Applicants note that the phrase "positioned for expression" is

defined at page 12 (lines 7-10). Given this definition, the rejection of claim 36 should be withdrawn.

Claim 36 was further deemed indefinite in reciting the phrase "under conditions for expressing." This rejection has been met by the present amendment to claim 36 in which this phrase has been replaced with the phrase "to express."

Claim 40 was deemed indefinite in reciting the term "including." This rejection has been met by the present amendment to claim 40 in which this term has been replaced with the term "comprising."

Claim 40 was also deemed indefinite because the phrase "said nucleic acid" lacks proper antecedent basis. This rejection has been met by the present amendment suggested by the Examiner, which amends the phrase to read " said nucleic acid molecule."

Claim 40 was further deemed indefinite in reciting the phrase "positioned for expression in the plant cell." As is discussed above, applicants note that this phrase is defined at page 12 (lines 7-12) of the specification. Given this definition, the rejection of claim 40 should be withdrawn.

Claim 40 was also deemed indefinite in reciting the term "growing." This rejection has been met by the present amendment to claim 40 suggested by the Examiner, in which the term "regenerating" replaces "growing."

Rejection under 35 U.S.C. § 101

Claims 17-21 were rejected under 35 U.S.C. § 101 as being directed to non-statutory subject matter. This rejection has been met by amending claim 17 to recite the term "transgenic."

Rejection under 35 U.S.C. § 102(b)

Claims 1, 2, 4-13, 15-29, 36, and 40-42 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Ryals *et al.* (WO 95/19443, 1995). This rejection has been met by the present amendments.

In particular, amended claims 1 and 10-12 (and their dependent claims) are now directed to isolated nucleic acid molecules encoding acquired resistance polypeptides possessing ankyrin repeats. These claims now incorporate the limitations of claims 3 and 14, which were found by the Examiner to be allowable over the Ryals reference. The rejection of the claims under § 102(b) may therefore be withdrawn.

Rejection under 35 U.S.C. § 102(e)

Claims 1-4, 6-24, 26, 28-29, 36, and 40-42 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Zhang *et al.* (U.S. Patent 5,623,054). In particular, the Office Action states:

[T]he polypeptide of Zhang directly interacts with polypeptides involved in

> pathogen resistance, and it is expected that the polypeptide comprises an ankyrin repeat because it was isolated by a yeast trap system using an *Arabidopsis* ankyrin repeat protein as a bait (col. 6, lines 43-61). It is also expected that the isolated nucleic [acid] molecules of Zhang would hybridize to SEQ ID NO: 1, 2, or 13 under low stringency conditions.

This rejection is respectfully traversed.

Claims 1 and 10-12, as amended, are directed to isolated nucleic acid molecules encoding acquired resistance polypeptides possessing ankyrin repeats. In view of this amendment, this rejection may be withdrawn.

As an initial matter, applicants note that there is no scientific basis for assuming that a bait protein of the yeast interaction trap system that includes an *Arabidopsis* ankyrin repeat protein will necessarily interact with polypeptides possessing ankyrin repeats, as apparently asserted in the present Office Action.

Moreover, applicants also point out that the use of the *Arabidopsis* ankyrin repeat bait protein in the interaction trap system of Zhang resulted in the isolation of the *Arabidopsis* 14-3-3 protein (see, e.g., col. 7, lines 50-51). Zhang, however, never discloses or suggests that the 14-3-3 protein includes ankyrin repeats. Consistent with this fact, applicants themselves have been unable to identify the presence of an ankyrin repeat in the 14-3-3 protein (SEQ ID NO: 2).

Finally, absent the presence of an ankyrin repeat in the Zhang 14-3-3 protein, it is unreasonable to assume that these 14-3-3 nucleic acid molecules would hybridize to applicants' claimed nucleic acid molecules under low stringency conditions, as asserted in

the Office Action.

For all of the above reasons, the § 102(e) rejection may be withdrawn.

Rejection under 35 U.S.C. § 103(a)

Claims 1-4, 6-29, 36, and 40-42 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Zhang *et al.* (U.S. Patent 5,623,054). Relying on the lack of novelty shown by the Zhang reference under § 102(e), the Office Action states:

> [I]t would have been *prima facie* obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the invention of Zhang to produce other transgenic plants than the disclosed tobacco plants, including cruciferous plants or monocots, because that would allow enhancement of pathogen resistance in other plant species. Plant transformation techniques were well known to one of skill in the art at the time of Applicant's invention as disclosed by Zhang (col. 17-18), and it would have been obvious to substitute one plant species for another because different plant species are functional equivalents and it would have been obvious to substitute one functional equivalent for another. It also would have been obvious to modify the method of Zhang to enhance resistance to other plant pathogens including *Phytophyhora, Perenospora or Pseudomonas*, because all of these are significant plant pathogens. The isolated nucleic acid molecules of Zhang confer general pathogen resistance by mediating signal transduction events leading to enhanced plant defense mechanisms and hence would be expected to be effective against a wide variety of pathogens. One would have had a reasonable expectation of success in view of the success of Zhang.

This rejection is respectfully traversed.

The present rejection is apparently based on the mistaken view that Zhang teaches a disease resistance gene falling within applicants' claims because the 14-3-3 protein is

expected to possess ankyrin repeats. To address this rejection, applicants refer to the discussion above providing reasons for the novelty of the claimed invention and the discussion of the Zhang reference. This discussion explains that Zhang simply does not disclose any member of applicants' claimed ankyrin repeat-containing plant disease resistance gene family. In the absence of such a teaching, the Zhang disclosure of the 14-3-3 protein cannot provide the presently claimed nucleic acid molecules, cells, plants, seeds, or associated methods. Indeed, absent applicants' disclosure, in which these genes are identified and described for the first time, one skilled in the art could hardly find obvious the genes themselves or their use for producing the claimed disease resistant transgenic plants.

Moreover, nothing in the Zhang reference would lead one to believe that applicants' claimed gene family would be useful for rendering plants disease resistant. Contrary to the assertion in the Office Action, the additional teachings of the Zhang reference regarding plant transformation and the involvement of the 14-3-3 protein in plant defense mechanisms add nothing of significance to the description of the 14-3-3 gene itself. Indeed, if one reading Zhang sought to confer disease resistance in a plant, there would be no need to look beyond the 14-3-3 sequence—which Zhang states is itself involved in plant disease resistance—much less to a completely different disease resistance gene family, such as the family discovered by applicants. The Zhang reference simply does not supply applicants' ankyrin repeat-containing genes, nor does it supply the

motivation or the direction for isolating such genes. Applicants request reconsideration on this issue and withdrawal of the § 103(a) rejection.

Conclusion

In view of the foregoing remarks, applicants submit that the claims are now in condition for allowance, and such action is respectfully requested.

If there are any additional charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 6/7/99

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